

5 I Claim:

1. A method for detecting kalikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15 associated with endocrine cancer in a patient comprising:
 - 10 (a) obtaining a sample from a patient;
 - (b) detecting or identifying in the sample kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15; and
 - (c) comparing the detected amounts with amounts detected for a standard.
2. A method of assessing whether a patient is afflicted with or has a pre-disposition for endocrine cancer, the method comprising comparing:
 - 15 (a) levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in a sample from the patient; and
 - (b) levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in samples of the same type obtained from control subjects, wherein significantly altered levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 relative to the corresponding levels from control subjects of kallikrein 12, kallikrein 14 and/or kallikrein or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 is an indication that the patient is afflicted with endocrine cancer.
- 25 3. A method of claim 1 or 2 wherein levels of kallikrein 14 are compared to levels from control normal subjects and higher levels of kallikrein 14 relative to the levels for normal subjects is an indication that the patient is afflicted with breast or ovarian cancer.
4. A method for monitoring the progression of endocrine cancer in a patient the method comprising:
 - 30 (a) detecting kallikrein 12, kallikrein 14, and/or kallikrein 15 proteins or nucleic acids encoding the proteins in a sample from the patient at a first time point;
 - (b) repeating step (a) at a subsequent point in time; and
 - (c) comparing the levels detected in (a) and (b), and therefrom monitoring the progression of the endocrine cancer.
5. A method for assessing the aggressiveness or indolence of an endocrine cancer, the method comprising comparing:
 - 35 (a) levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in a patient sample; and
 - (b) levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in a control sample, wherein a significant difference between the levels in the patient sample and levels in a control sample is an indication that the cancer is aggressive or indolent.
- 40 6. A method for determining whether an endocrine cancer has metastasized or is likely to metastasize

- 5 in the future, the method comprising comparing:
- (a) levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in a patient sample; and
 - (b) non-metastatic levels of kallikrein 12, kallikrein 14 and/or kallikrein 15 or nucleic acids encoding kallikrein 12, kallikrein 14 and/or kallikrein 15 in a control sample.
- 10 7. A method for diagnosing and monitoring ovarian carcinoma in a subject comprising measuring kallikrein 12, kallikrein 14, and/or kallikrein 15 in a sample from the subject.
8. A method as claimed in any preceding claim wherein the kallikrein 12, kallikrein 14, and/or kallikrein 15 is measured using antibodies specifically reactive with kallikrein 12, kallikrein 14, and/or kallikrein 15 or a part thereof.
- 15 9. A method for screening a subject for endocrine cancer comprising (a) obtaining a biological sample from a subject; (b) detecting the amount of kallikrein 12, kallikrein 14, and/or kallikrein 15 in said sample; and (c) comparing said amount of kallikrein 12, kallikrein 14, and/or kallikrein 15 detected to a predetermined standard, where detection of a level of kallikrein 12, kallikrein 14, and/or kallikrein 15 significantly different than that of a standard is indicative of endocrine cancer.
- 20 10. A method of claim 9 wherein levels of kallikrein 14 are compared with normal levels and higher levels of kallikrein 14 in the sample compared with the normal levels is indicative of ovarian cancer or breast cancer.
11. A method of claim 10 comprising
- (a) incubating a biological sample from the subject with a first antibody specific for kallikrein 12, kallikrein 14, and/or kallikrein 15 which is directly or indirectly labeled with a detectable substance, and a second antibody specific for kallikrein 12, kallikrein 14, and/or kallikrein 15 which is immobilized;
 - (b) detecting the detectable substance thereby quantitating kallikrein 12, kallikrein 14, and/or kallikrein 15 in the biological sample; and
 - (c) comparing the quantitated kallikrein 12, kallikrein 14, and/or kallikrein 15 with levels for a predetermined standard.
- 25 12. A method for diagnosing and monitoring endocrine cancer in a sample from a subject comprising isolating nucleic acids, preferably mRNA, from the sample, and detecting *KLK12*, *KLK14*, and/or *KLK15* nucleic acids in the sample.
- 30 13. A method as claimed in claim 12 wherein the presence of different levels of *KLK12*, *KLK14*, and/or *KLK15* nucleic acids in the sample compared to a standard or control is indicative of disease, disease stage, and/or prognosis.
14. A method for determining the presence or absence of ovarian cancer in a subject comprising (a) contacting a sample obtained from the subject with an oligonucleotide that hybridizes to *KLK12*, *KLK14*, and/or *KLK15*; and (b) detecting in the sample a level of polynucleotide that hybridizes to the *KLK12*, *KLK14*, and/or *KLK15* relative to a predetermined cut-off value, and therefrom determining the presence or absence of ovarian cancer in the subject.
- 40 15. A method as claimed in claim 14, wherein the polynucleotide is mRNA and the level of

- 5 polynucleotide is detected by polymerase chain reaction.
16. A method as claimed in claim 14 wherein the polynucleotide is mRNA and the amount of mRNA is detected using a hybridization technique, employing oligonucleotide probes that hybridize to KLK12, KLK14, and/or KLK15, or a complement of KLK12, KLK14, and/or KLK15.
17. A method of claim 16 comprising (a) contacting a sample obtained from the subject with
10 oligonucleotides that hybridize to one or both of KLK14 or KLK15; and (b) detecting in the sample levels of polynucleotides that hybridize to one or both of KLK14 or KLK15 relative to a predetermined cut-off value, and therefrom determining the presence or absence of ovarian cancer in the subject.
18. A method of claim 12 or 13 wherein one or both of KLK14 and KLK15 mRNA is detected by (a)
15 isolating mRNA from a sample and combining the mRNA with reagents to convert it to cDNA; (b) treating the converted cDNA with amplification reaction reagents and nucleic acid primers that hybridize to one or both of KLK14 and KLK15, to produce amplification products; (d) analyzing the amplification products to detect amounts of one or both of KLK14 and KLK15 mRNA; and (e) comparing the amounts of mRNA to amounts detected against a panel of expected values for
20 normal and malignant tissue derived using similar nucleic acid primers.
19. A method of any preceding claim wherein higher levels of KLK14 in patients compared to a control is indicative of early stage disease (Grade I or II), optimal debulking, longer progression free disease and overall survival, and/or that the subject is responsive to chemotherapy.
20. A method of any preceding claim wherein higher levels of KLK15 in patients compared to a control
25 are indicative of ovarian cancer.
21. A method of any preceding claim wherein higher levels of KLK15 in patients compared to a control are indicative of reduced progression free survival and overall survival.
22. An *in vivo* method for imaging ovarian cancer comprising:
30 (a) injecting a patient with an agent that binds to kallikrein 12, kallikrein 14, and/or kallikrein 15, the agent carrying a label for imaging the cancer;
(b) allowing the agent to incubate *in vivo* and bind to kallikrein 12, kallikrein 14, and/or kallikrein 15 associated with the cancer; and
(c) detecting the presence of the label localized to the cancer.
23. A method of assessing the potential of a test compound to contribute to endocrine cancer
35 comprising:
(a) maintaining separate aliquots of endocrine cancer diseased cells in the presence and absence of the test compound; and
(b) comparing levels of kallikrein 12, kallikrein 14, and/or kallikrein 15 proteins or nucleic acids encoding the proteins in each of the aliquots, and wherein a significant difference in levels of
40 kallikrein 12, kallikrein 14, and/or kallikrein 15 proteins or nucleic acids encoding the proteins in the presence of the test compound relative to the aliquots maintained in the absence of the test compound is an indication that the test compound has potential to contribute to endocrine cancer..
24. A method for assessing the potential efficacy of a test agent for inhibiting endocrine cancer in a

- 5 patient, the method comprising comparing:
- (a) levels of kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15, and optionally other endocrine cancer markers in a first sample obtained from a patient and exposed to the test agent; and
- 10 (b) levels of kallikrein 12, kallikrein 14, and/or kallikrein 15 and optionally other markers in a second sample obtained from the patient, wherein the sample is not exposed to the test agent, wherein a significant difference in the levels of expression of kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15, and optionally the other markers in the first sample, relative to the second sample, is an indication that the test agent is potentially efficacious for inhibiting
- 15 endocrine cancer in the patient.
25. A method of assessing the efficacy of a therapy for inhibiting endocrine cancer in a patient comprising comparing: (a) levels of kallikrein 12, kallikrein 14, and/or kallikrein 15 proteins or nucleic acids encoding the proteins in a sample from the patient obtained from the patient prior to providing at least a portion of the therapy to the patient; and (b) levels of kallikrein 12, kallikrein 20 14, and/or kallikrein 15 or nucleic acids encoding the proteins in a second sample obtained from the patient following therapy.
26. A method of identifying or selecting an agent for inhibiting endocrine cancer in a patient comprising:
- (a) obtaining a sample from the patient;
- 25 (b) separately maintaining aliquots of the sample in the presence of a plurality of test agents;
- (c) comparing kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15, and optionally other endocrine cancer markers, in each of the aliquots; and
- 30 (d) selecting one of the test agents which alters the levels of kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15, and optionally other endocrine cancer markers, in the aliquot containing that test agent, relative to other test agents.
27. A method of inhibiting endocrine cancer in a patient comprising:
- (a) obtaining a sample comprising diseased cells from the patient;
- 35 (b) separately maintaining aliquots of the sample in the presence of a plurality of test agents;
- (c) comparing levels of kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15 in each aliquot;
- 40 (d) administering to the patient at least one of the test agents which alters the levels of the kallikrein 12, kallikrein 14, and/or kallikrein 15, and/or nucleic acids encoding kallikrein 12, kallikrein 14, and/or kallikrein 15 in the aliquot containing that test agent, relative to the other test agents.
28. A method of any preceding claim wherein the sample comprises serum.
29. A method of any preceding claim wherein the endocrine cancer is ovarian cancer.

- 84 -

- 5 30. A diagnostic composition comprising a kallikrein 12, kallikrein 14, and/or kallikrein 15 protein, an agent that binds to a kallikrein 12, kallikrein 14, and/or kallikrein 15 protein, KLK12, KLK14, and/or KLK15, or probes or primers that hybridize to KLK12, KLK14, and/or KLK15.
31. Use of kallikrein 12, kallikrein 14, and/or kallikrein 15 in the preparation of a pharmaceutical composition for treating ovarian cancer.
- 10 32. A kit for carrying out a method as claimed in any preceding claim.
33. A kit for determining the presence of ovarian or breast cancer in a patient comprising a known amount of a binding agent that specifically binds to kallikrein 14 wherein the binding agent comprises a detectable substance or it binds directly or indirectly to a detectable substance.
- 15 34. A kit for determining the presence of ovarian cancer in a patient comprising a known amount of an oligonucleotide that binds to one or both of KLK14 and KLK15 wherein the oligonucleotide is directly or indirectly labeled with a detectable substance.
35. A kit for assessing the suitability of each of a plurality of agents for inhibiting ovarian cancer in a patient the kit comprising a plurality of agents and reagents for detecting kallikrein 14, KLK14, and/or KLK15.
- 20 36. A method of conducting a drug discovery business comprising:
- (a) providing a method as claimed in claim 26 for identifying an agent that inhibits endocrine cancer in a patient;
 - (b) conducting therapeutic profiling of agents identified in step (a), or further analogs thereof, for efficacy and toxicity in animals; and
 - 25 (c) formulating a pharmaceutical preparation including one or more agents identified in step (b) as having an acceptable therapeutic profile.